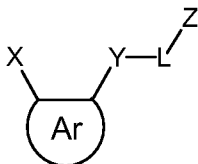


## AMENDMENT TO THE SPECIFICATION

Please replace paragraphs [0021]-[0070] with the following amended paragraphs:

[0021] The present invention comprises a compound for modulating kinase activity, particularly Tie-2, of Formula I,



I

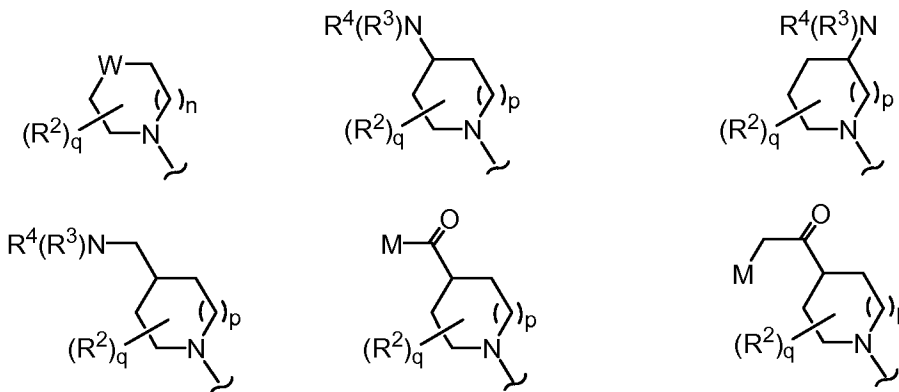
or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is a five- to six-membered aromatic ring system containing between one and three heteroatoms, said five- to six-membered aromatic ring system substituted with -X and -Y-L-Z, in an ortho relationship to each other, and said five- to six-membered aromatic ring system optionally substituted with up to four R<sup>1</sup>;

each R<sup>1</sup> is independently selected from -H, halogen, -CN, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, -OC(O)R<sup>3</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

optionally two of R<sup>1</sup>, together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of R<sup>1</sup>;

X is selected from the following six formulae:



wherein,

W is selected from  $-C(R^2)(R^2)-$ ,  $-N(R^4)-$ ,  $-S(O)_{0-2}-$ , and  $-O-$ ;

n = 1 or 2;

p = 0 or 1;

q is 1 to 3;

M is  $-OR^3$  or  $-N(R^3)R^4$ ;

each  $R^2$  is independently selected from -H, halogen, oxo, -CN,  $-NH_2$ ,  $-NO_2$ ,  $-OR^3$ ,  $-N(R^3)R^3$ ,  $-N(R^3)R^5$ ,  $-S(O)_{0-2}R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ ,  $-N(R^3)SO_2R^3$ ,  $-N(R^3)C(O)R^3$ ,  $-N(R^3)CO_2R^3$ ,  $-N(R^3)C(O)N(R^3)R^3$ ,  $-C(O)R^3$ ,  $-OC(O)R^3$ , optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl;

two of  $R^2$ , together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each  $R^3$  is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl; or

two of  $R^3$ , when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocycl ring, said optionally substituted five- to seven-membered heterocycl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each  $R^4$  is independently selected from  $R^3$ ,  $-SO_2R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ , and  $-C(O)R^3$ ;

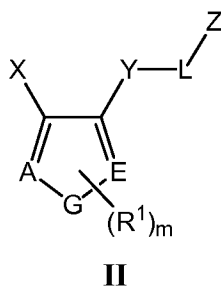
Y is selected from  $-CH_2-$ ,  $-O-$ ,  $-S(O)_{0-2}-$ ,  $-N(R^3)-$ , and absent;

L is selected from  $-(CH_2)_{1-3}-$ ,  $-(CH_2)_{1-3}N(R^3)-$ ,  $-(CH_2)_{1-3}O-$ ,  $-(CH_2)_{1-3}S(O)_{0-2}-$  and absent; each of the aforementioned methylenes optionally substituted;

Z is a five- to seven-membered ring system or  $-R^3$ , said five- to seven-membered ring system optionally substituted with zero to four of  $R^5$ ; and

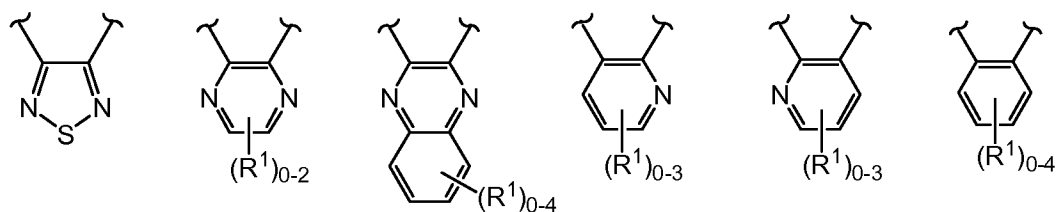
$R^5$  is selected from -H, halogen, -CN, oxo, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>4</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl; and optionally two of  $R^5$ , together with the atoms to which they are attached, form a second ring system fused with said five- to seven-membered ring system, said second ring system substituted with zero to four of  $R^5$ , hereinafter embodiment [0021].

**[0022]** In one example, the compound is according to embodiment paragraph [0021], having formula **II**,



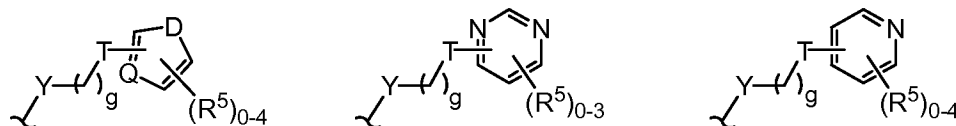
wherein, A and E are each independently N or -C(R<sup>1</sup>)-; and G is selected from -S(O)<sub>0-2</sub>-, and -C(R<sup>1</sup>)=C(R<sup>1</sup>)-, hereinafter embodiment [0022].

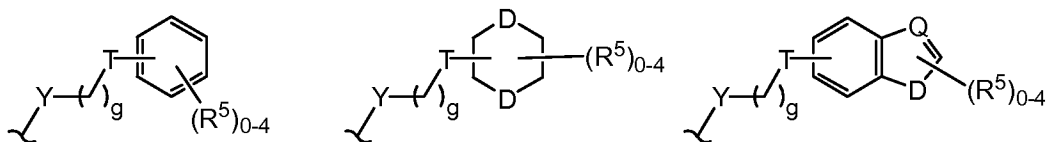
**[0023]** In another example, the compound is according to embodiment paragraph [0022], wherein Ar is selected from the following formulae:-



hereinafter embodiment [0023].

**[0024]** In another example, the compound is according to embodiment paragraph [0023], wherein -Y-L-Z is selected from the following formulae,

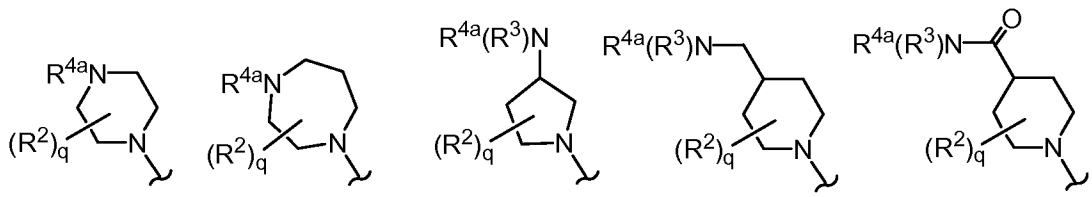




wherein g is zero to two; D is selected from  $-C(R^5)(R^5)-$ ,  $-O-$ ,  $-S(O)_{0-2}-$ , and  $-N(R^4)-$ ; Q is  $=N-$  or  $-C(R^5)-$ ; T is selected from absent,  $-N(R^3)-$ ,  $-S-$  and  $-O-$ ; and each methylene between Y and T is optionally substituted; provided that when both Y and T are heteroatoms then g must be two, hereinafter embodiment [0024].

[0025] In another example, the compound is according to embodiment paragraph [0024], wherein Y is  $-O-$  or optionally substituted  $-CH_2-$ , hereinafter embodiment [0025].

[0026] In another example, the compound is according to embodiment paragraph [0025], wherein X is selected from the following formulae:



hereinafter embodiment [0026]

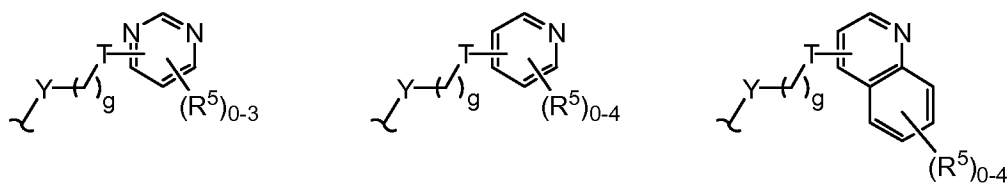
[0027] In another example, the compound is according to embodiment paragraph [0026], wherein  $R^{4a}$  is selected from  $-SO_2R^3$ ,  $-SO_2N(R^3)R^4$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ , and  $-C(O)R^3$ , hereinafter embodiment [0027].

[0028] In another example, the compound is according to embodiment paragraph [0027], wherein each  $R^2$  is independently selected from  $-H$  or optionally substituted lower alkyl, hereinafter embodiment [0028].

[0029] In another example, the compound is according to embodiment paragraph [0028], wherein each  $R^2$  is independently selected from  $-H$ , haloalkyl,  $-C_{1-6}alkyl-N(R^3)R^3$ ,  $-C_{1-6}alkyl-OR^3$ ,  $-C_{1-6}alkyl-CO_2R^3$ , and  $-C_{1-6}alkyl-C(O)N(R^3)R^3$ , hereinafter embodiment [0029].

[0030] In another example, the compound is according to embodiment paragraph [0029], wherein  $R^{4a}$  is  $-C(O)N(R^3)R^3$  or  $-C(O)R^3$ , hereinafter embodiment [0030].

[0031] In another example, the compound is according to embodiment paragraph [0030], wherein  $-Y-L-Z$  is selected from the following formulae,

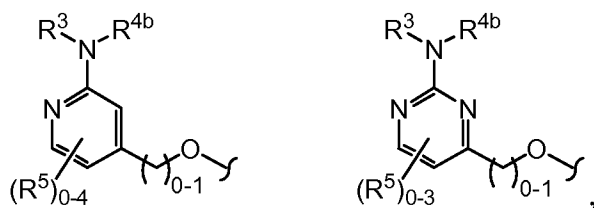


wherein Y, T, and g are as described above, hereinafter embodiment [0031].

**[0032]** In another example, the compound is according to embodiment paragraph [0031], wherein g is one or two, hereinafter embodiment [0032].

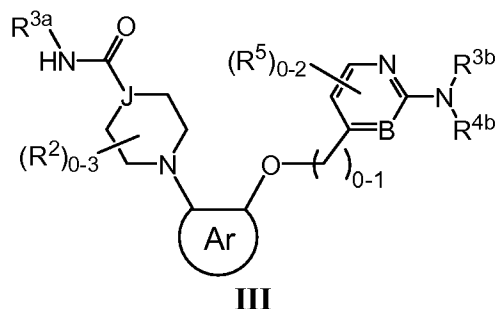
**[0033]** In another example, the compound is according to embodiment paragraph [0032], wherein each  $R^5$  is independently selected from -H, halogen, -CN, -NH<sub>2</sub>, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>4</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, and optionally substituted lower alkyl, hereinafter embodiment [0033].

**[0034]** In another example, the compound is according to embodiment paragraph [0033], wherein -Y-L-Z is selected from the following formulae:



hereinafter embodiment [0034]

**[0035]** In another example, the compound is according to embodiment paragraph [0034], having formula **III**,



wherein J is N or CH, and B is =N- or =C(R<sup>5</sup>)-, hereinafter embodiment [0035].

**[0036]** In another example, the compound is according to embodiment paragraph [0035], wherein R<sup>3a</sup> is selected from optionally substituted aryl, optionally substituted lower arylalkyl, optionally

substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl, hereinafter embodiment [0036].

[0037] In another example, the compound is according to embodiment paragraph [0036], wherein  $R^{3a}$  is selected from optionally substituted aryl and optionally substituted heteroaryl, hereinafter embodiment [0037].

[0038] In another example, the compound is according to embodiment paragraph [0037], wherein  $R^{3a}$  is optionally substituted phenyl, hereinafter embodiment [0038].

[0039] In another example, the compound is according to embodiment paragraph [0038], wherein said optionally substituted phenyl is substituted with at least one of halogen, -CN, -CF<sub>3</sub>, -NH<sub>2</sub>, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, optionally substituted lower alkyl, and optionally substituted aryl, hereinafter embodiment [0039].

[0040] In another example, the compound is according to embodiment paragraph [0039], wherein said optionally substituted phenyl group is substituted with at least one trifluoromethyl group, hereinafter embodiment [0040].

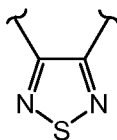
[0041] In another example, the compound is according to embodiment paragraph [0040], wherein said optionally substituted phenyl group is substituted with at least two trifluoromethyl groups, hereinafter embodiment [0041].

[0042] In another example, the compound is according to embodiment paragraph [0039], wherein said optionally substituted phenyl group is substituted with at least one lower alkyl group, hereinafter embodiment [0042].

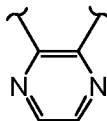
[0043] In another example, the compound is according to embodiment paragraph [0039], wherein  $R^{3b}$  is -H, hereinafter embodiment [0043].

[0044] In another example, the compound is according to embodiment paragraph [0043], wherein  $R^{4b}$  is selected from R<sup>3</sup>, -H, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>4</sup>, and -C(O)R<sup>3</sup>, hereinafter embodiment [0044].

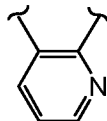
[0045] In another example, the compound is according to embodiment paragraph [0044], wherein Ar is according to the formula below, hereinafter embodiment [0045].



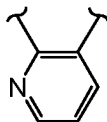
[0046] In another example, the compound is according to ~~embodiment paragraph~~ [0044], wherein Ar is according to the formula below, hereinafter embodiment [0046].



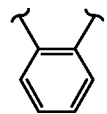
[0047] In another example, the compound is according to ~~embodiment paragraph~~ [0044], wherein Ar is according to the formula below, hereinafter embodiment [0047].



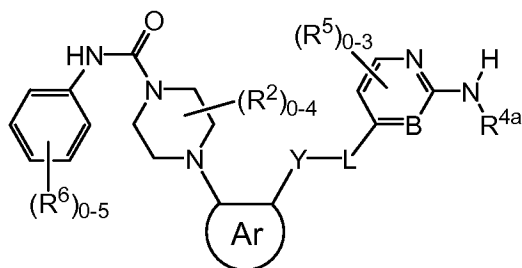
[0048] In another example, the compound is according to ~~embodiment paragraph~~ [0044], wherein Ar is according to the formula below, hereinafter embodiment [0048].



[0049] In another example, the compound is according to ~~embodiment paragraph~~ [0044], wherein Ar is according to the formula below, hereinafter embodiment [0049].



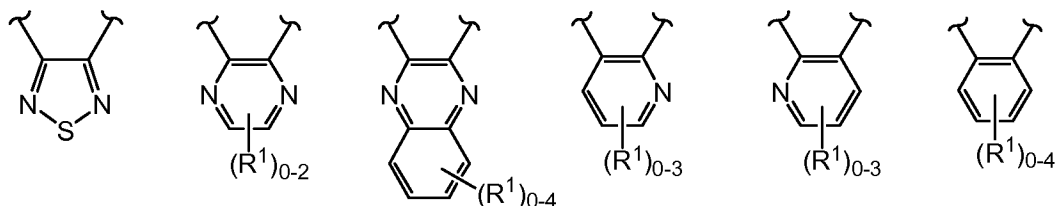
[0050] In another example, the present invention comprises a compound for modulating kinase activity, particularly Tie-2, of Formula IV,



#### IV

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is selected from the following formulae:



each  $R^1$  is independently selected from -H, halogen, -CN, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; optionally two of  $R^1$ , together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of  $R^1$ ;

each  $R^2$  is independently selected from -H, halogen, oxo, -CN, -NH<sub>2</sub>, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)R<sup>5</sup>, -S(O)<sub>0-2</sub>R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>3</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>3</sup>, -N(R<sup>3</sup>)C(O)N(R<sup>3</sup>)R<sup>3</sup>, -C(O)R<sup>3</sup>, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

two of  $R^2$ , together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each  $R^3$  is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of  $R^3$ , when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;



each  $R^4$  is independently selected from  $R^3$ ,  $-SO_2R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ , and  $-C(O)R^3$ ;

Y is selected from optionally substituted  $-CH_2-$ ,  $-O-$ ,  $-S-$ , and  $-N(R^3)-$ ;

L is selected from optionally substituted  $-CH_2-$ ,  $-O-$ ,  $-S-$ ,  $-N(R^3)-$  and absent;

provided that Y and L are not both heteroatoms;

B is  $=N-$  or  $=C(H)-$ ;

at each instance,  $R^5$  and  $R^6$  are independently selected from  $-H$ , halogen,  $-CN$ ,  $-NO_2$ ,  $-OR^3$ ,  $-N(R^3)R^4$ ,  $-S(O)_{0-2}R^3$ ,  $-SO_2N(R^3)R^3$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^3$ ,  $-N(R^3)SO_2R^3$ ,  $-N(R^3)C(O)R^3$ ,  $-N(R^3)CO_2R^3$ ,  $-C(O)R^3$ , optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl; and

optionally two of  $R^5$ , together with the atoms to which they are attached, form a ring system fused with the ring containing B according to formula **IV**, said ring system substituted with zero to two additional of  $R^5$ , hereinafter embodiment [0050].

**[0051]** In another example, the compound is according to embodiment paragraph [0050], wherein Y is  $-O-$  and L is optionally substituted  $-CH_2-$ , hereinafter embodiment [0051].

**[0052]** In another example, the compound is according to embodiment paragraph [0051], wherein at least one of  $R^6$  is optionally substituted lower alkyl, hereinafter embodiment [0052].

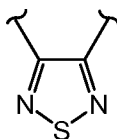
**[0053]** In another example, the compound is according to embodiment paragraph [0052], wherein said at least one optionally substituted lower alkyl is *meta*- to the piperazine urea function as depicted in formula **IV**, hereinafter embodiment [0053].

**[0054]** In another example, the compound is according to embodiment paragraph [0053], wherein  $R^{4a}$  is selected from  $R^3$ ,  $-H$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ , and  $-C(O)R^3$ , hereinafter embodiment [0054].

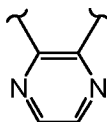
**[0055]** In another example, the compound is according to embodiment paragraph [0054], wherein  $R^{4a}$  is selected from  $-H$ ,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ , and  $-C(O)R^3$ , hereinafter embodiment [0055].

**[0056]** In another example, the compound is according to embodiment paragraph [0055], wherein  $-Y-L-$  is  $-OCH_2-$ , hereinafter embodiment [0056].

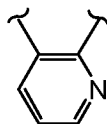
[0057] In another example, the compound is according to ~~embodiment paragraph~~ [0056], wherein Ar is according to the formula below, hereinafter embodiment [0057].



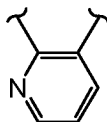
[0058] In another example, the compound is according to ~~embodiment paragraph~~ [0056], wherein Ar is according to the formula below, hereinafter embodiment [0058].



[0059] In another example, the compound is according to ~~embodiment paragraph~~ [0056], wherein Ar is according to the formula below, hereinafter embodiment [0059].



[0060] In another example, the compound is according to ~~embodiment paragraph~~ [0056], wherein Ar is according to the formula below, hereinafter embodiment [0060].

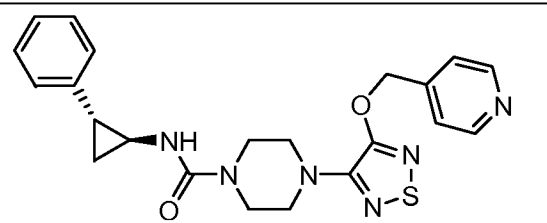
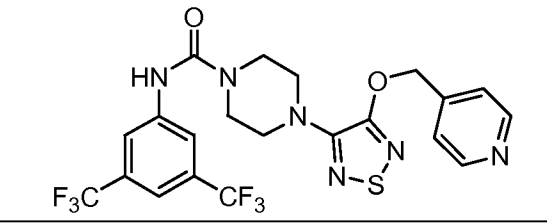
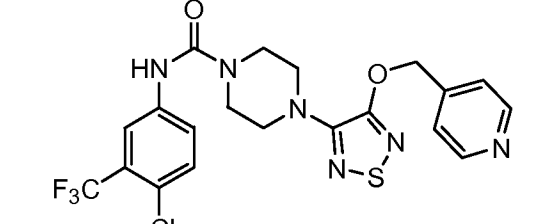
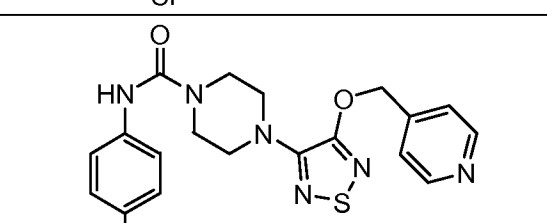
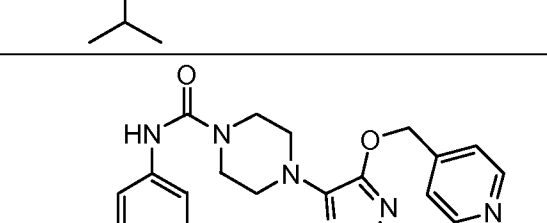
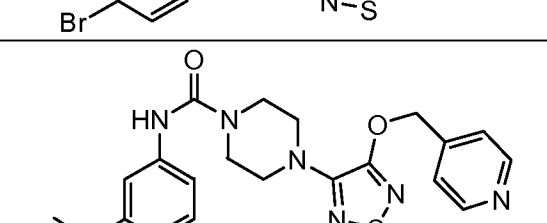
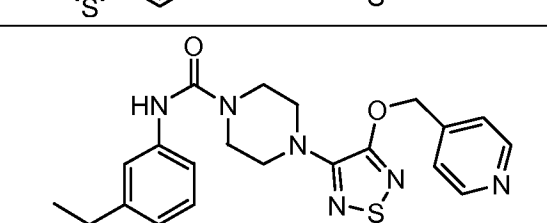


[0061] In another example, the compound is according to ~~embodiment paragraph~~ [0056], wherein Ar is according to the formula below, hereinafter embodiment [0061].



[0062] In another example, the compound is according to ~~embodiment paragraph~~ [0021], selected from Table 1, hereinafter embodiment [0062].

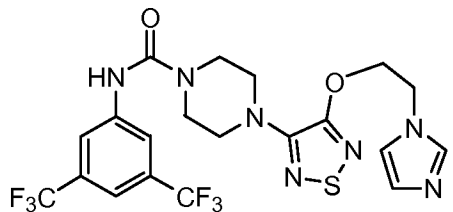
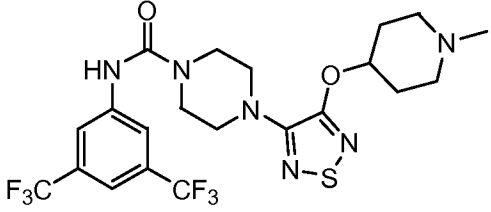
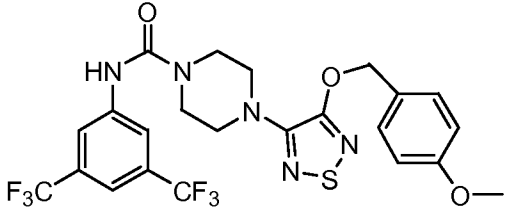
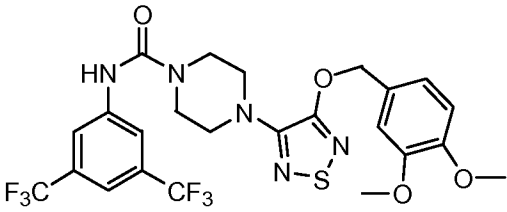
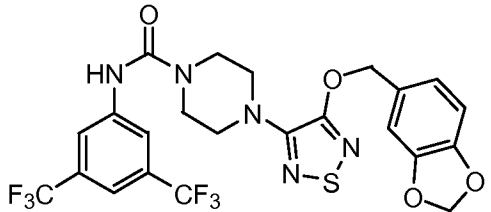
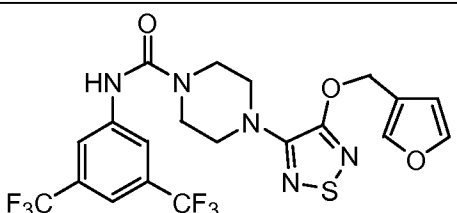
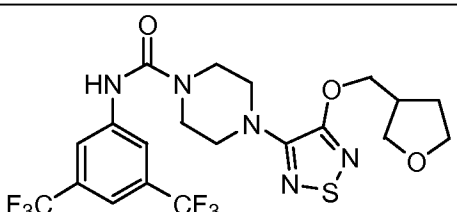
**Table 1**

1	N-[(1R,2S)-2-phenylcyclopropyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
2	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
3	N-[4-chloro-3-(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
4	N-[4-(1-methylethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
5	N-(3-bromophenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
6	N-[3-(methylthio)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
7	N-(3-ethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

**Table 1**

8	N-(3,5-dimethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
9	N-[3-trifluoromethylphenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
10	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-methylquinolin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
11	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(3-(dimethylamino)phenyl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
12	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(1H-indol-5-yl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
13	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(3-thienylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
14	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-morpholin-4-ylethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

**Table 1**

15	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-{[2-(1H-imidazol-1-yl)ethyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
16	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(1-methylpiperidin-4-yl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
17	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[4-(methyloxy)phenyl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
18	4-[4-({[3,4-bis(methyloxy)phenyl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
19	4-{4-[(1,3-benzodioxol-5-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
20	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(furan-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
21	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(tetrahydrofuran-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

**Table 1**

22	N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
23	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-1,4-diazepane-1-carboxamide	
24	1-({[(1S,2R,5S)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy}acetyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
25	5-phenyl-N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)-1,3-oxazole-4-carboxamide	
26	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-4-{[3-(trifluoromethyl)phenyl]acetyl}piperazine	
27	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(piperidin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
28	N-[3,5-bis(trifluoromethyl)phenyl]-N'-[(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperidin-4-yl)methyl]urea	

**Table 1**

29	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(3-pyridin-3-ylpropyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
30	N-[3,5-bis(trifluoromethyl)phenyl]-4-{1,1-dioxido-4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
31	4-[4-(1-azabicyclo[2.2.2]oct-3-yloxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
32	4-[(4-[(3,5-bis(trifluoromethyl)phenyl)amino]carboxyl)oxy]methyl]benzoic acid	
33	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(piperidin-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
34	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-pyrrolidin-1-ylethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
35	4-{4-[(2-amino-2-methylpropyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	

**Table 1**

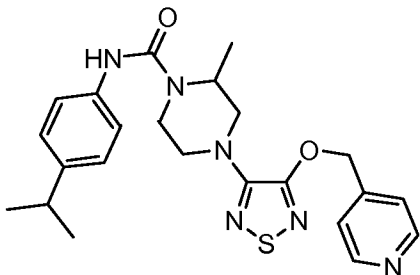
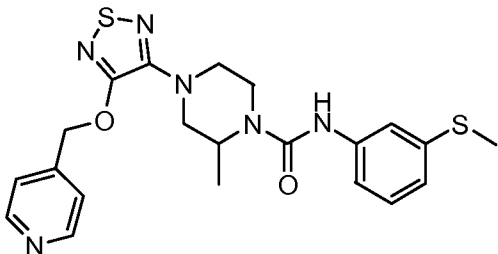
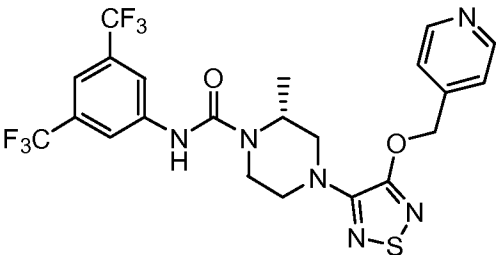
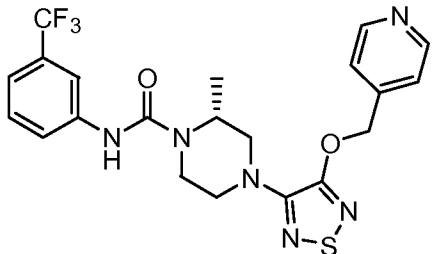
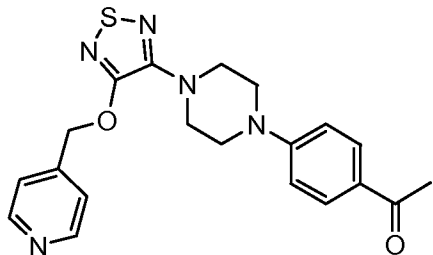
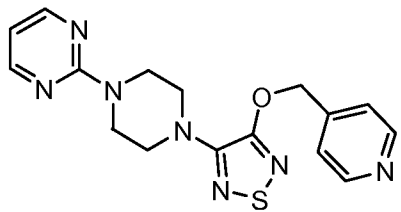
36	N-[3,5-bis(trifluoromethyl)phenyl]-1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperidine-4-carboxamide	
37	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperidine-4-carboxamide	
38	N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
39	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
40	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-piperidin-4-ylethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
41	2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
42	1-phenyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	



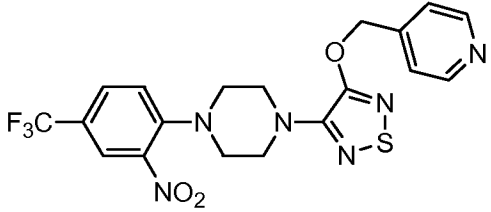
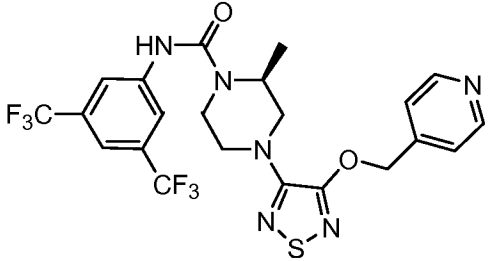
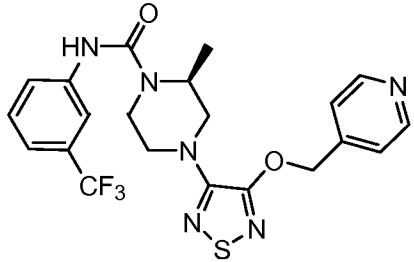
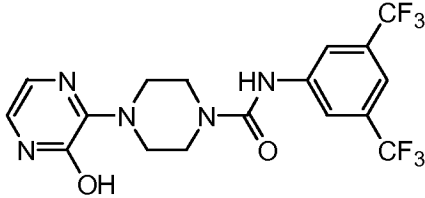
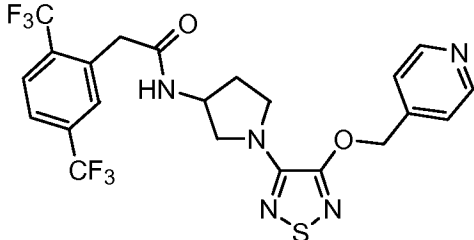
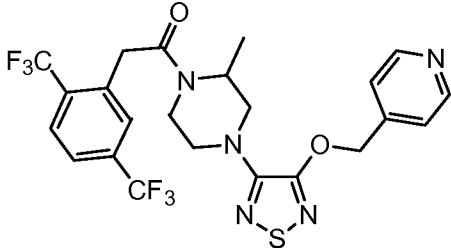
**Table 1**

43	1-[(4-methylphenyl)methyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
44	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)amino]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
45	4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]-1,4-diazepane-1-carboxamide	
46	2-methyl-1-{[2-(methyloxy)phenyl]carbonyl}-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
47	N-[5-chloro-2-(methyloxy)phenyl]-N'-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)urea	
48	N-[5-methyl-2-(methyloxy)phenyl]-N'-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)urea	
49	N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)-N'-[3-(trifluoromethyl)phenyl]urea	

**Table 1**

50	2-methyl-N-[4-(1-methylethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
51	2-methyl-N-[3-(methylthio)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
52	(2R)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
53	(2R)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
54	1-[4-(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazin-1-yl)phenyl]ethanone	
55	2-(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazin-1-yl)pyrimidine	

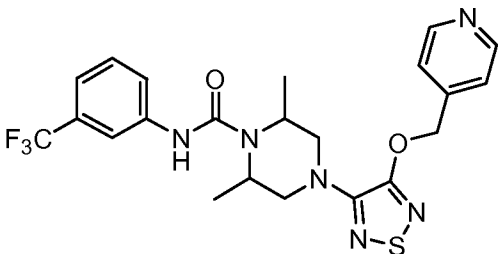
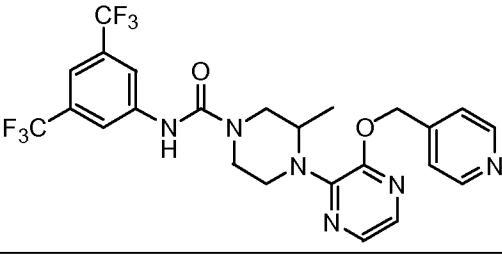
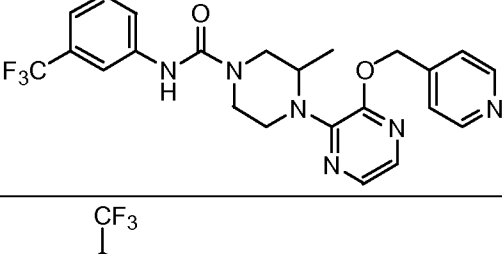
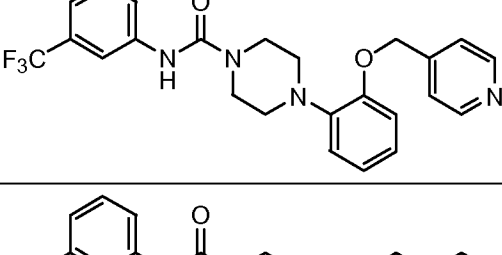
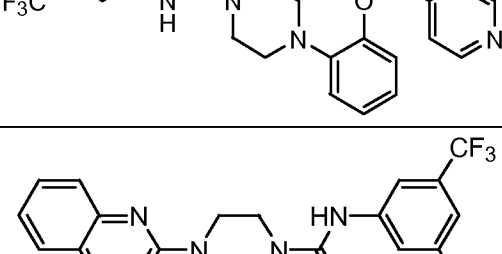
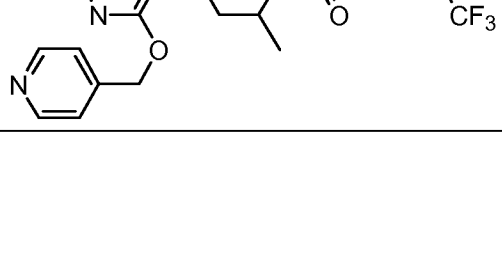
**Table 1**

56	1-[2-nitro-4-(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
57	(2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
58	(2S)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
59	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-hydroxypyrazin-2-yl)piperazine-1-carboxamide	
60	2-[2,5-bis(trifluoromethyl)phenyl]-N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)acetamide	
61	1-{[2,5-bis(trifluoromethyl)phenyl]acetyl}-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	

**Table 1**

62	N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
63	2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
64	N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
65	2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
66	N-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)-N'-[3-(trifluoromethyl)phenyl]urea	
67	N-[3,5-bis(trifluoromethyl)phenyl]-N'-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)urea	
68	N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

**Table 1**

69	2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
70	N-[3,5-bis(trifluoromethyl)phenyl]-3-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
71	3-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
72	N-[3,5-bis(trifluoromethyl)phenyl]-4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}piperazine-1-carboxamide	
73	4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
74	N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}piperazine-1-carboxamide	

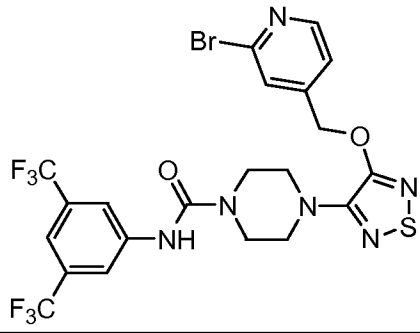
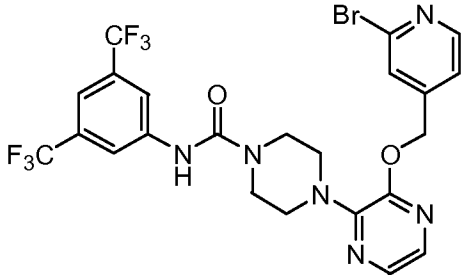
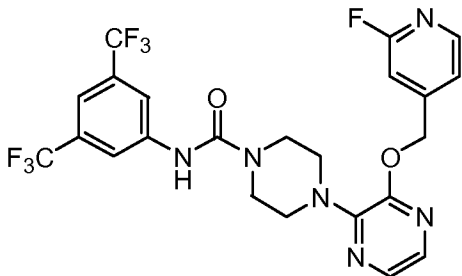
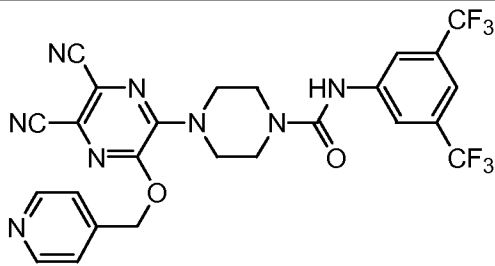
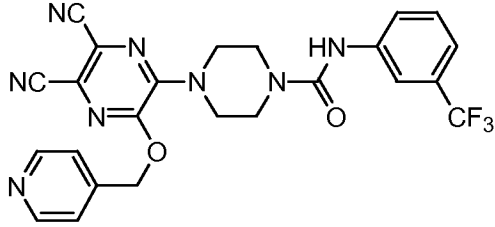
**Table 1**

75	N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-1,4-diazepane-1-carboxamide	
76	2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
77	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]-1,4-diazepane-1-carboxamide	
78	N-[3,5-bis(trifluoromethyl)phenyl]-2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
79	2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
80	(2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
81	(2S)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

**Table 1**

82	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-fluoropyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	
83	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-chloropyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	
84	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-chloropyridin-4-yl)methyl]oxy}pyrazin-2-yl)piperazine- 1-carboxamide	
85	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2- {[(2,3,5,6-tetrafluoropyridin-4-yl) amino]methyl}phenyl)piperazine-1- carboxamide	
86	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2- {[(3-chloro-2,5,6-trifluoropyridin-4-yl) amino]methyl}phenyl)piperazine-1- carboxamide	

**Table 1**

87	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-bromopyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	
88	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-bromopyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- 1-carboxamide	
89	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-fluoropyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- 1-carboxamide	
90	N-[3,5-bis(trifluoromethyl)phenyl]-4- {5,6-dicyano-3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-carboxamide	
91	4-{5,6-dicyano-3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	



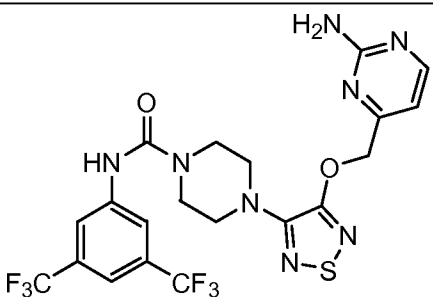
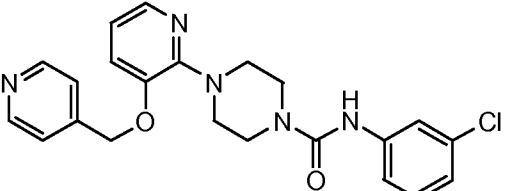
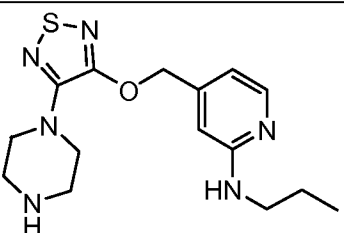
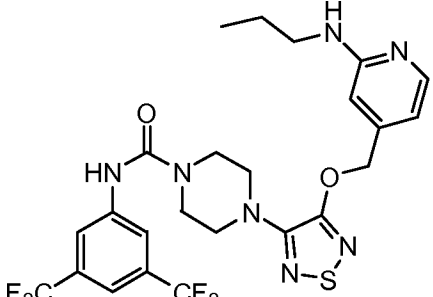
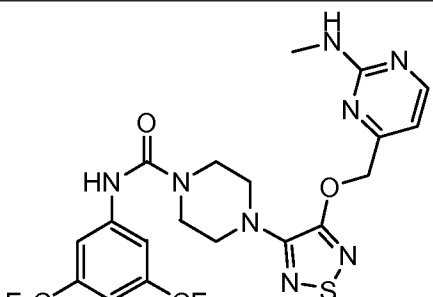
**Table 1**

92	N-(3-ethylphenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
93	N-(3-ethylphenyl)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
94	N-(3-ethylphenyl)-2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
95	N-(3-ethylphenyl)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}piperazine-1-carboxamide	
96	N-[3,5-bis(trifluoromethyl)phenyl]-4-[3-(2-pyridin-4-ylethyl)pyrazin-2-yl]piperazine-1-carboxamide	
97	N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide	

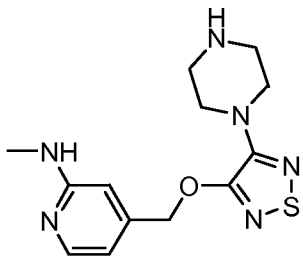
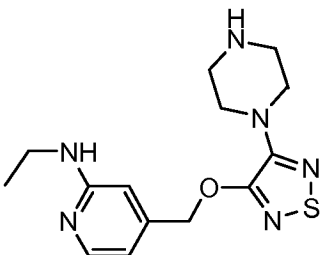
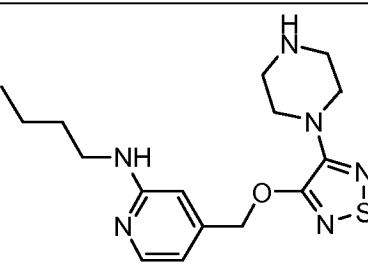
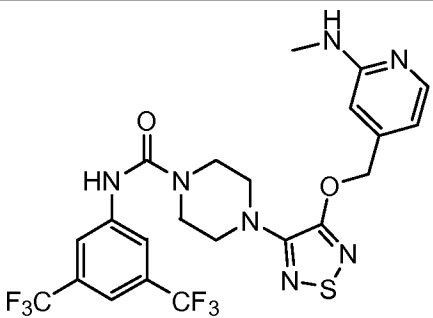
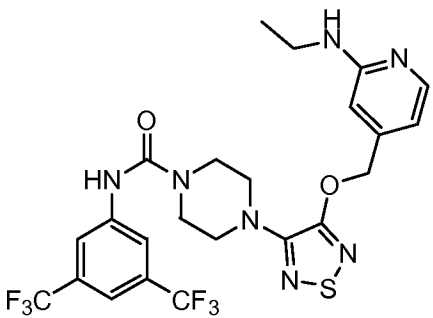
**Table 1**

98	N-[3,5-bis(trifluoromethyl)phenyl]-4-{2-[(pyridin-4-yloxy)methyl]phenyl}piperazine-1-carboxamide	
99	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
100	1,1-dimethylethyl {4-[(4-{4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-yl} carbamate	
101	methyl {4-[(4-{4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-yl} carbamate	
102	4-{[(4-piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-amine	
103	N-(4-chlorophenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide	

**Table 1**

104	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
105	N-(3-chlorophenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide	
106	4-{{(4-piperazin-1-yl)-1,2,5-thiadiazol-3-yl}oxy}methyl}-N-propylpyridin-2-amine	
107	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(propylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
108	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(methylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	

**Table 1**

109	N-methyl-4- {[ (4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	
110	N-ethyl-4- {[ (4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	
111	N-butyl-4- {[ (4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	
112	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(methylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
113	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(ethylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	

**Table 1**

114	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(butylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
115	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(phenylmethyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
116	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(1-methylethyl)amino]pyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
117	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(phenylmethyl)amino]pyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
118	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(phenylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	

**Table 1**

119	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[2-( (dimethylamino)ethyl]amino}pyrimidin- 4-yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	
120	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[2-( (dimethylamino)ethyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	
121	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(ethylamino)pyrimidin-4- yl]methyl]oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	
122	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(propylamino)pyrimidin-4- yl]methyl]oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	
123	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(cyclopropylamino)pyrimidin-4- yl]methyl]oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	

**Table 1**

124	4-[4-({[2-(acetylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
125	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(phenylcarbonyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
126	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(phenylcarbonyl)amino]pyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
127	4-{4-[(2-[bis(phenylcarbonyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	

**Table 1**

128	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(cyclopentylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
129	4-[4-({[2-(acetylaminopyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
130	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl)amino]pyridin-4-yl}methyl}oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
131	methyl {4-[(4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl}pyrimidin-2-yl} carbamate	
132	4-(4-({[2-(aminopyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-(3-ethylphenyl)piperazine-1-carboxamide	



**Table 1**

133	methyl [4-({[4-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-yl]carbamate	
134	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-{[(2-cyanopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
135	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
136	4-[(4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl]pyrimidine-2-carboxamide	
137	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(butyloxy)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	

### Table 1

138	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyrimidin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
139	4-[(4-{4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl]pyridine-2-carboxylic acid	
140	2-pyrrolidin-1-ylethyl 4-[(4-{4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl]pyridin-2-yl} carbamate	
141	2-morpholin-4-ylethyl 4-[(4-{4-[(3,5-bis(trifluoromethyl)phenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy)methyl]pyridin-2-yl} carbamate	
142	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	

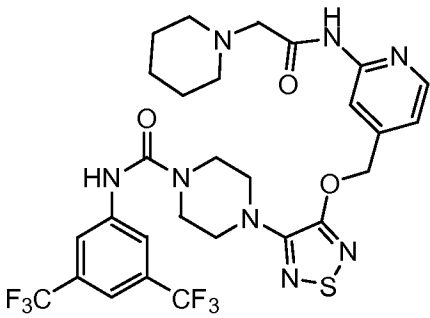
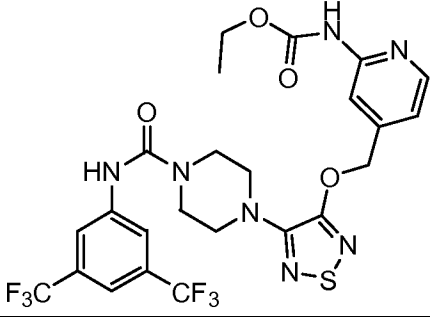
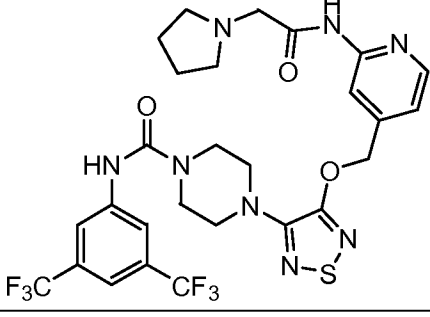
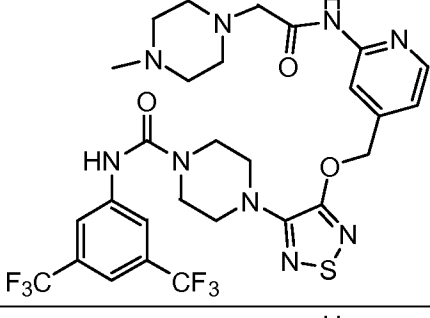
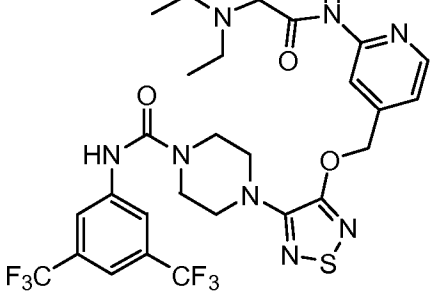
**Table 1**

143	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[(1-methylpiperidin-3- yl)carbonyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	
144	4-(3-{{(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-(3- ethylphenyl)piperazine-1-carboxamide	
145	2-(4-methylpiperazin-1-yl)ethyl 4-[(4- [4-({[3,5- bis(trifluoromethyl)phenyl]amino}carbo nyl)piperazin-1-yl]-1,2,5-thiadiazol-3- yl}oxy)methyl]pyridin-2-yl} carbamate	
146	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[(1-ethylpiperidin-4- yl)carbonyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	

**Table 1**

147	4-(4-{{(2-aminopyridin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-{{3-[(trifluoromethyl)thio]phenyl}piperazine-1-carboxamide	
148	4-({[4-(4-{{3,5-bis(trifluoromethyl)phenyl}sulfonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-amine	
149	4-(4-{{(2-aminopyridin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-naphthalen-1-ylpiperazine-1-carboxamide	
150	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(N,N-dimethylglycyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
151	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(morpholin-4-yl)acetyl]amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

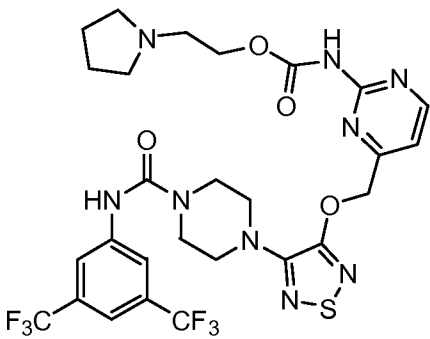
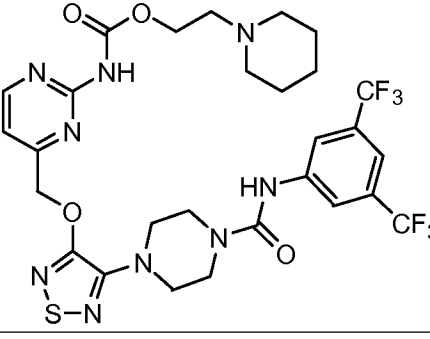
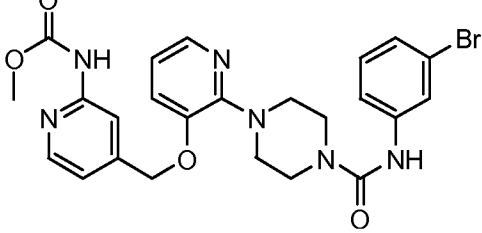
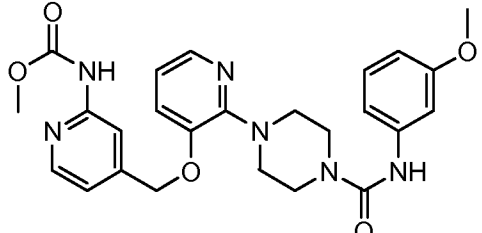
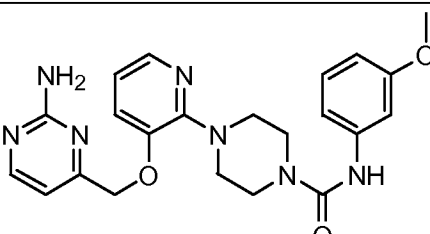
**Table 1**

152	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(piperidin-1-yl)acetyl]amino)pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
153	ethyl {4-[(4-[4-({3,5-bis(trifluoromethyl)phenyl}amino)carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl]oxy)methyl}pyridin-2-yl} carbamate	
154	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(pyrrolidin-1-yl)acetyl]amino)pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
155	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-{[(2-[(4-methylpiperazin-1-yl)acetyl]amino)pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
156	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(N,N-diethylglycyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

**Table 1**

157	1-ethylpiperidin-4-yl {4-[(4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl} carbamate	
158	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
159	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(2-oxo-1,3-oxazolidin-3-yl)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
160	2-(diethylamino)ethyl {4-[(4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl} carbamate	
161	methyl [4-({[2-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate	

**Table 1**

162	2-pyrrolidin-1-ylethyl {4-[(4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl} carbamate	
163	2-piperidin-1-ylethyl {4-[(4-[4-([3,5-bis(trifluoromethyl)phenyl]amino)carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl} carbamate	
164	methyl {4-[(2-[4-[(3-bromophenyl)amino]carbonyl]piperazin-1-yl)pyridin-3-yl]oxy}methyl]pyridin-2-yl} carbamate	
165	methyl {4-[(2-[4-[(3-methoxyphenyl)amino]carbonyl]piperazin-1-yl]pyridin-3-yl]oxy}methyl]pyridin-2-yl} carbamate	
166	4-(3-[(2-aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-[3-(methoxyphenyl)]piperazine-1-carboxamide	

**Table 1**

167	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	
168	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-{3-[(trifluoromethyl)oxy]phenyl}piperazine-1-carboxamide	
169	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
170	N-(3-ethylphenyl)-4-[3-({[2-({[3-ethylphenyl]amino}carbonyl)amino]pyridin-4-yl)methyl}oxy]pyridin-2-yl]piperazine-1-carboxamide	
171	N-(3-ethylphenyl)-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide	



**Table 1**

172	N-(3-ethylphenyl)-4-(4-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
173	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide	
174	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
175	4-[3-({[2-(acetyl amino)pyridin-4-yl]methyl}oxy)pyridin-2-yl]-N-(3-ethylphenyl)piperazine-1-carboxamide	
176	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	

**Table 1**

177	2-[4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)piperazin-1-yl]-N-[3,5-bis(trifluoromethyl)phenyl]acetamide	
178	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-phenylpiperazine-1-carboxamide	
179	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	
180	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
181	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	

### Table 1

182	2-(4-methylpiperazin-1-yl)ethyl [4-( {[2-(4- {[3-ethylphenyl]amino}carbonyl}piperazin-1-yl)pyridin-3-yl]oxy} methyl)pyridin-2-yl]carbamate	
183	4-(3- {[ (2-aminopyrimidin-4-yl)methyl]oxy} pyridin-2-yl)-N-(3-chlorophenyl)piperazine-1-carboxamide	
184	4-(3- {[ (2-aminopyrimidin-4-yl)methyl]oxy} pyridin-2-yl)-N-(3-bromophenyl)piperazine-1-carboxamide	
185	N-[4-( {[2-(4-acetylpiperazin-1-yl)pyridin-3-yl]oxy} methyl)pyridin-2-yl]-2-(4-methylpiperazin-1-yl)acetamide	
186	4-(3- {[ (2-aminopyrimidin-4-yl)methyl]oxy} pyridin-2-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide	
187	4-(3- {[ (2-aminopyrimidin-4-yl)methyl]oxy} pyridin-2-yl)-N-(4-fluorophenyl)piperazine-1-carboxamide	

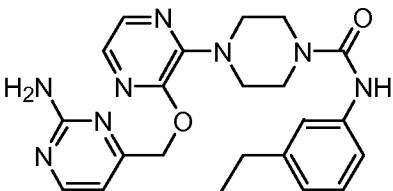
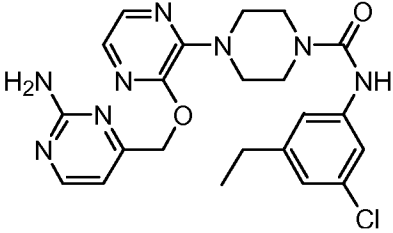
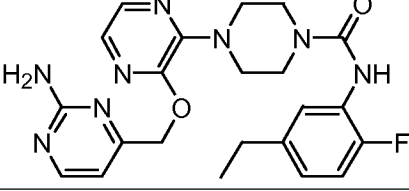
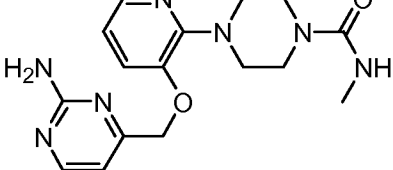
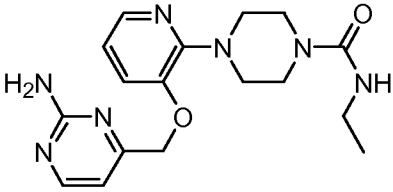
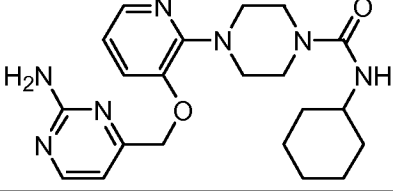
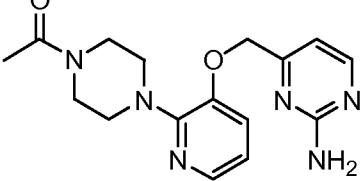
**Table 1**

188	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(2-fluorophenyl)piperazine-1-carboxamide	
189	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	
190	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
191	N-methyl-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide	
192	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
193	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide	
194	4-(3-{{(2-amino-5-bromopyrimidin-4-yl)methyl}oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	

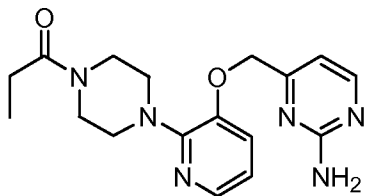
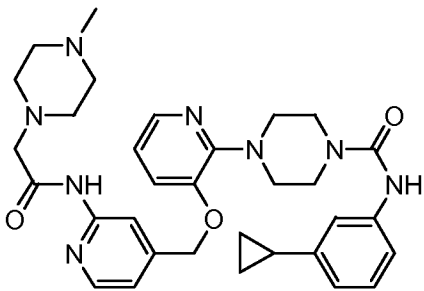
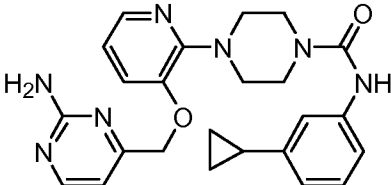
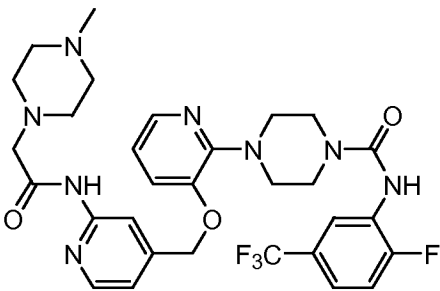
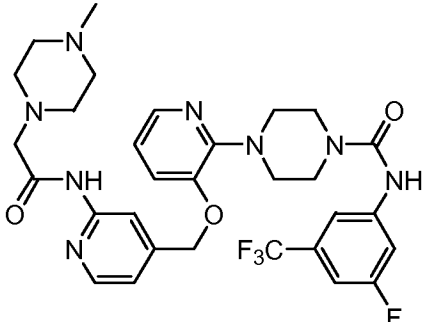
**Table 1**

195	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-fluoro-3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
196	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
197	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
198	N-(3-chloro-5-ethylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
199	N-(5-ethyl-2-fluorophenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
200	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

**Table 1**

201	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
202	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	
203	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
204	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-methylpiperazine-1-carboxamide	
205	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-ethylpiperazine-1-carboxamide	
206	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-cyclohexylpiperazine-1-carboxamide	
207	4-({[2-(4-acetylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine	

**Table 1**

208	4-([2-(4-propanoylpiperazin-1-yl)pyridin-3-yl]oxy)methylpyrimidin-2-amine	
209	N-(3-cyclopropylphenyl)-4-(3-([2-((4-methylpiperazin-1-yl)acetyl)amino]pyridin-4-yl)methyl]oxy)pyridin-2-yl)piperazine-1-carboxamide	
210	4-(3-([2-(aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-(3-cyclopropylphenyl)piperazine-1-carboxamide	
211	N-[2-fluoro-5-(trifluoromethyl)phenyl]-4-(3-([2-((4-methylpiperazin-1-yl)acetyl)amino]pyridin-4-yl)methyl]oxy)pyridin-2-yl)piperazine-1-carboxamide	
212	N-[3-fluoro-5-(trifluoromethyl)phenyl]-4-(3-([2-((4-methylpiperazin-1-yl)acetyl)amino]pyridin-4-yl)methyl]oxy)pyridin-2-yl)piperazine-1-carboxamide	

### Table 1

213	N-(3,5-dichlorophenyl)-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide	
214	4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
215	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	
216	4-(3-{{1-(2-aminopyrimidin-4-yl)ethyl}oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
217	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
218	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	



**Table 1**

219	4-[(2-[4-(3,4-dihydroquinolin-1(2H)-ylcarbonyl)piperazin-1-yl]pyridin-3-yl)oxy)methyl]pyrimidin-2-amine	
220	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-methylpropyl)piperazine-1-carboxamide	
221	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	
222	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
223	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
224	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-phenylpiperazine-1-carboxamide	
225	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

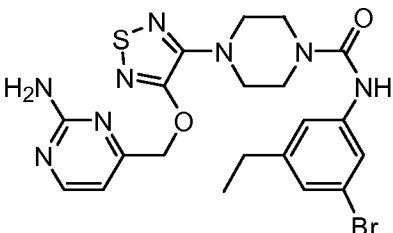
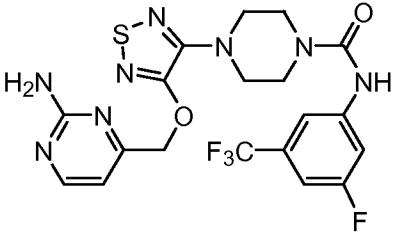
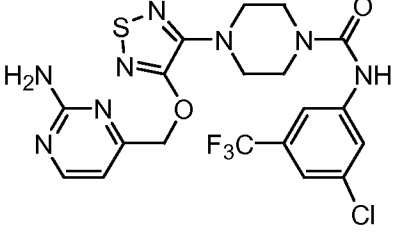
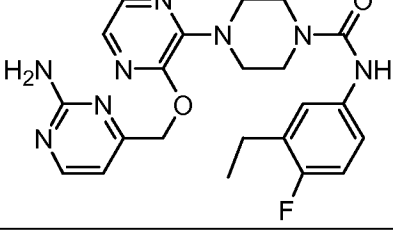
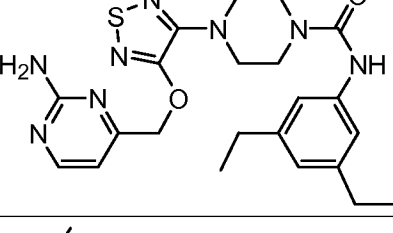
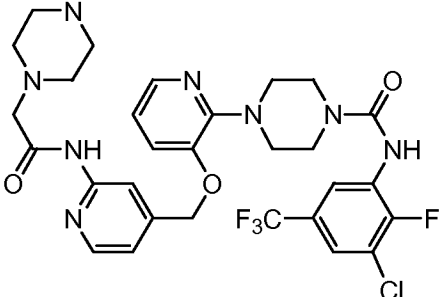
**Table 1**

226	N-(3,5-diethylphenyl)-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)oxy}methyl}pyridin-2-yl)piperazine-1-carboxamide	
227	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}-6-methylpyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
228	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}-6-methylpyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
229	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
230	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-phenylpiperazine-1-carboxamide	
231	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

**Table 1**

232	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
233	N-[3-chloro-5-(trifluoromethyl)phenyl]-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide	
234	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
235	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
236	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	
237	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}-6-chloropyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	

**Table 1**

238	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	
239	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
240	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
241	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	
242	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	
243	N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]-4-(3-{{(2-{{(4-methylpiperazin-1-yl)acetyl}amino}pyridin-4-yl)methyl}oxy}pyridin-2-yl)piperazine-1-carboxamide	

**Table 1**

244	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
245	4-(3-{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
246	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
247	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-ethyl-5-fluorophenyl)piperazine-1-carboxamide	
248	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
249	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

**Table 1**

250	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]-N-methylpiperazine-1-carboxamide	
251	4-(3-{{(2-aminopyrimidin-4-yl)methyl}oxy}pyrazin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	
252	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	
253	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-4-fluorophenyl)piperazine-1-carboxamide	
254	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[2,5-bis(methoxy)phenyl]piperazine-1-carboxamide	
255	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
256	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-(3-ethylphenyl)piperazine-1-carboxamide	

**Table 1**

257	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide	
258	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-{3-[(trifluoromethyl)oxy]phenyl}piperazine-1-carboxamide	
259	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide	
260	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
261	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	
262	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
263	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide	

**Table 1**

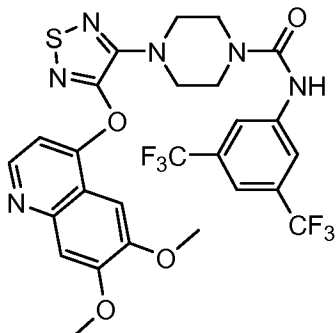
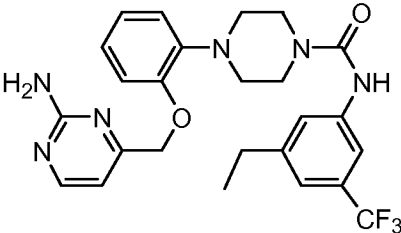
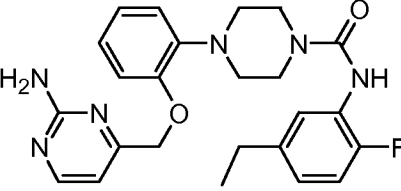
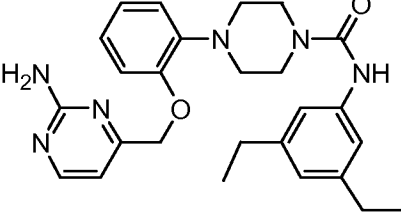
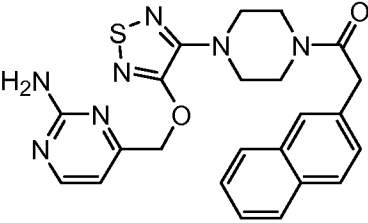
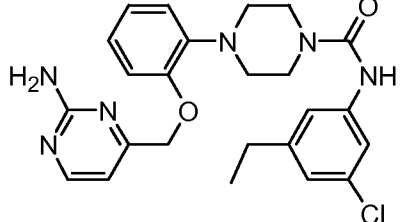
264	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[2-(ethoxy)phenyl]piperazine-1-carboxamide	
265	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-(3,4-difluorophenyl)piperazine-1-carboxamide	
266	4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(methylthio)phenyl]piperazine-1-carboxamide	
267	N-(3-acetylphenyl)-4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
268	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
269	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-(3-fluorophenyl)piperazine-1-carboxamide	
270	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-phenylpiperazine-1-carboxamide	



**Table 1**

271	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
272	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
273	4-[4-({[6,7-bis(methoxy)quinolin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
274	4-({[4-(4-{[3,5-bis(trifluoromethyl)phenyl]acetyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyrimidin-2-amine	
275	5-{{(2-aminopyrimidin-4-yl)methyl}oxy}-6-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]pyrazine-2-carboxamide	

**Table 1**

276	4-(4-{[6,7-bis(methoxy)quinolin-4-yl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
277	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
278	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
279	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	
280	4-[(4-{4-[4-(naphthalen-2-ylacetyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-amine	
281	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	

[0063] Another aspect of the invention is a pharmaceutical composition comprising the compound according to any one of ~~embodiments~~~~paragraphs~~ [0021]-[0062] and a pharmaceutically acceptable carrier, hereinafter embodiment [0063].

[0064] Another aspect of the invention is a metabolite of the compound or the pharmaceutical composition according to any one of ~~embodiments~~~~paragraphs~~ [0021]-[0063], hereinafter embodiment [0064].

[0065] Another aspect of the invention is a method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of a composition comprising at least one of the compound according to any of ~~embodiments~~~~paragraphs~~ [0021]-[0062] and the pharmaceutical composition according to ~~embodiment~~~~paragraph~~ [0063], hereinafter embodiment [0065].

[0066] Another aspect of the invention is the method according to ~~embodiment~~~~paragraph~~ [0065], wherein the kinase is Tie-2, hereinafter embodiment [0066].

[0067] Another aspect of the invention is the method according to ~~embodiment~~~~paragraph~~ [0066], wherein modulating the *in vivo* activity of Tie-2 comprises inhibition of Tie-2.

[0068] Another aspect of the invention is a method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of a composition comprising at least one of the compound according to any of ~~embodiments~~~~paragraphs~~ [0021]-[0062] and the pharmaceutical composition according to ~~embodiment~~~~paragraph~~ [0063].

[0069] Another aspect of the invention is a method of screening for modulator of a Tie-2 kinase, the method comprising combining either a composition comprising at least one of the compound according to any of ~~embodiments~~~~paragraphs~~ [0021]-[0062] and the pharmaceutical composition according to ~~embodiment~~~~paragraph~~ [0063], and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.

[0070] Another aspect of the invention is a method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of at least one of the compound according to any of ~~embodiments~~~~paragraphs~~ [0021]-[0062] and the pharmaceutical composition according to ~~embodiment~~~~paragraph~~ [0063].